

## REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1-103 under 35 U.S.C. § 112 (1<sup>st</sup> para.) for lack of written descriptive support is respectfully traversed in view of the above amendments and the following remarks.

It is the position of the U.S. Patent and Trademark Office (“PTO”) that the amendments to claim 1, filed December 22, 2005 and October 20, 2006, introducing provisos lack written descriptive support and are new matter, because no support was found in the specification for such provisos. Applicants submit that this rejection is obviated in view of the above amendments removing the proviso language from claim 1.

Moreover, the PTO argues that the present application lacks written descriptive support for all compounds encompassed by the claims and asserts that claims 1-103 lack adequate written descriptive support, because the specification does not present a sufficient variety of species to reflect the variance in the broad genus as instantly claimed. The PTO also asserts that there is no disclosure of a correlation between the function and structure of the compounds beyond the compounds disclosed in the few examples in the specification. In addition, the PTO argues that the Declaration of Bruce Molino, Ph.D. Under 37 CFR §1.132 submitted in response to the previous office action is insufficient to overcome the rejection because percent inhibition data for the compounds compared directly with the positive control (CsA) are not expressed in the same units.

Applicants respectfully disagree. There is more than ample basis for a claim of the scope of currently amended claim 1. First, the present application is clearly directed to cyclosporin analogue compounds of the type claimed by the amended claims. Specific compounds according to the claimed invention are set forth in Examples 19-23, 25-29, 31-42, 45-63, 65, 67-73, 75, 79-80, 85-97, and 108. This is more than sufficient to demonstrate that applicants had possession of the claimed invention. Moreover, applicants have filed herewith a Supplemental Declaration of Bruce Molino, Ph.D. Under 37 C.F.R. § 1.132 (“Supplemental Molino Declaration”). The Supplemental Molino Declaration clearly compares inhibition data for compounds of the present invention (IC<sub>50</sub> µg/mL in column 5) with inhibition by

positive control CsA ( $IC_{50}$   $\mu\text{g/mL}$  in column 6) in the same units. In addition, the  $IC_{50}$  values for the positive control are the concentration of the positive control (cyclosporin A) that inhibit  $[3\text{H}]$ -thymidine uptake by 50%, which may be compared with the percent inhibition for test compounds at 0.1  $\mu\text{g/mL}$  and 1.0  $\mu\text{g/mL}$  test concentrations (Supplemental Molino Declaration ¶7). The accompanying Supplemental Molino Declaration demonstrates that a significant number of compounds in accordance with the claimed invention have immunosuppressive activity.

Accordingly, the rejection under 35 U.S.C. § 112 (1<sup>st</sup> para.) for lack of written descriptive support is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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/Georgia Evans/  
Georgia Evans  
Registration No. 44,597

NIXON PEABODY LLP  
1100 Clinton Square  
Rochester, New York 14604  
Telephone: (312) 425-8565  
Facsimile: (312) 425-3909